

1124-95

Reticulated Platelets in Acute Coronary Syndrome: A Potential Marker for Platelet ConsumptionValeri Tsyboulev, J. Jorgensen, Abdus Saleem, Nasser M. Lakkis Baylor College of Medicine, Houston, TX

Introduction: The physiologic sequelae of damage to the vascular endothelium which include platelet adhesion to subendothelial elements in the blood vessel wall, recruitment of circulating platelets to form a hemostatic plug, and its subsequent consolidation with fibrin strands are now well established. We hypothesize that the presence of circulating reticulated (containing-RNA) platelets is potentially a reliable marker for platelet aggregation and thrombus formation in acute coronary syndrome.

Methods: Forty-seven subjects (15 controls, 32 patients with acute coronary syndrome) were studied. All patients had chest pain within 24 hours along with ischemic ST changes on the ECG or evidence of myocardial injury. Blood was collected for platelet count, mean platelet volume, and for flow cytometric analysis for the presence of reticulated platelets as assessed by uptake thiazole orange, and the expression of CD41a for the GPIIb/IIIa receptor on the platelet membrane. All studies were repeated in the presence of RNA-ase with evidence of 90% decrease of thiazole orange uptake.

Results: The mean platelet count was 220 ± 32 in the control group and 207 ± 45 in the acute coronary syndrome patients. The mean platelet volume was statistically higher in patients than in controls (10.6 ± 1 fl vs. 9.6 ± 0.5 fl, $p=0.008$). Sixteen percent of the overall platelet population was reticulated in the acute coronary syndrome group compared to only 3 percent in the control group. Patients admitted with ST-elevation acute coronary syndrome had more reticulated platelets than those with non-ST-elevation (21.3 ± 6.9 vs. 14.9 ± 6.9 , $p=0.01$). Also, diabetic patients presenting with acute coronary syndrome had a significantly higher percentage of circulating reticulated platelets compared to non-diabetic patients ($p=0.0003$). Aspirin seems to eliminate these differences.

Conclusion: Reticulated platelets appear to be a reliable marker for platelet aggregation and consumption in acute coronary syndrome. More studies are needed to further understand this novel observation.

1124-114

EARLY Platelet Substudy

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Background: Receptors other than GP IIb/IIIa may mediate leukocyte-platelet-endothelial interactions that obstruct the microvasculature in acute coronary syndromes (ACS) and cause microinfarcts. The effect of eptifibatide (EP) on these receptors was investigated in the EARLY trial. **Methods:** Platelet receptors (mean fluorescence intensity) and aggregation (10 μ mol ADP) were determined at baseline, and at 3, 6, 12 and 24 hours after randomization to early (E) (in the Emergency Department, $n=27$) or late (L) (12-24 hours, $n=28$) EP therapy. **Results:** Aggregation was inhibited by early EP (baseline, $72 \pm 20\%$; 3 hours post, $7 \pm 9\%$, $p<0.001$). CD31, CD63, CD 107a, CD 107b, CD 41 (GPIIb/IIIa expression), and CD 62p were not affected in either group. Leukocyte-platelet aggregates trended upward after presentation (early baseline, 43.1 ± 26.0 versus 65.8 ± 35.6 , $p=.09$). PAC-1 (GPIIb/IIIa activity), CD 51/61 (vitronectin receptor and CD 42b (GP Ib) were inhibited by EP ($p<0.05$). **Conclusion:** In Emergency Dept patients with ACS, EP rapidly and profoundly inhibits platelet aggregation and reduces GP IIb/IIIa activity and the expression of CD51/61 and CD 42b; the latter two effects may also contribute to the drug's anti-thrombotic effect. However, platelet-leukocyte aggregate formation, a marker of platelet activity rises within 24 hours after presentation despite eptifibatide therapy and is a potential mechanism for microvascular obstruction.

	CD 42b		PAC-1		CD51/61	
	E	L	E	L	E	L
Baseline	207 \pm 60	126 \pm 7	5.8 \pm 9	5.5 \pm 1	11.9 \pm 2	11.5 \pm 5
3H	121 \pm 40*	140 \pm 9	2.2 \pm 4*	4.9 \pm 2	5.9 \pm 3	10.8 \pm 3
6H	135 \pm 73*	117 \pm 5	2.4 \pm 1*	4.4 \pm 1	5.6 \pm 2	12.4 \pm 3
12H	129 \pm 62*	102 \pm 4	2.6 \pm 1*	3.7 \pm 7	6.1 \pm 2	12.9 \pm 3
24H	135 \pm 82*	107 \pm 5	2.3 \pm 4*	3.1 \pm 1	6.0 \pm 2	6.2 \pm 2.3

* $p<0.05$ vs. baseline + $p<0.05$ between groups

1124-115

Eptifibatide Provides Additional Platelet Inhibition in Non-ST Elevation Myocardial Infarction Patients Already Treated With Aspirin and Clopidogrel: Results of the PEACE Study

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Background: Thienopyridines and glycoprotein(Gp) IIb/IIIa antagonists have been tested separately with success in the treatment of non ST elevation myocardial infarction (NSTEMI). Although often co-prescribed in this context, the antiplatelet interaction of these agents is poorly described and the superiority of GpIIb/IIIa antagonists above

thienopyridine treatment alone is not clear. The hypothesis of the study was that eptifibatide offered further antiplatelet effect above clopidogrel in the medical stabilisation of NSTEMI prior to elective PCI.

Methods: 32 NSTEMI patients treated with aspirin and enoxaparin were studied using flow-cytometry to define parameters of platelet activation with a panel of agonists before clopidogrel, following clopidogrel and during an eptifibatide infusion.

Results: With ADP, TRAP and U46, relative reductions in PAC-1 expression (conformationally activated Gp IIb/IIIa receptor) of 51%, 46% and 39% (all $p<0.0001$) respectively were seen with clopidogrel but a further 85%, 84% and 72% (all $p<0.0001$) reduction was seen with eptifibatide. Fibrinogen binding was significantly reduced following clopidogrel by 77%, 63% and 69% (all $p<0.0001$) and again further reduced by 99%, 98% and 98% (all $p<0.0001$) with eptifibatide. The total number of GPIIb/IIIa receptors (P2) and P-selectin expression were also reduced following clopidogrel, with all agonists, ($p<0.026$, ADP and TRAP) however both parameters increased slightly in all cases with eptifibatide ($p<0.012$ with ADP).

Conclusion: The activated IIb/IIIa expression and fibrinogen binding findings indicate that eptifibatide provides significant potent antiplatelet activity above that of clopidogrel suggesting additive immediate protection in the treatment of NSTEMI. The P2 and P-selectin findings suggest the possibility of a partial agonist (and/or pro-inflammatory) effect, the consequences of which, with longer infusions are unknown.

1124-116

Predictors of Early Mortality From an Unselected Patient Registry of Acute Coronary Syndromes (TRACS)

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Background: Several stratification models exist to predict early and late complications from an acute coronary syndrome (ACS). Most of these models are based on patient populations selected from randomized clinical trials and most are used to predict composite outcomes. The goal of this study was to determine predictors of mortality as a solitary end point in an unselected cohort of patients presenting to the Emergency Department (ED) with an ACS.

Methods: The Registry of Acute Coronary Syndromes (TRACS) represents a dataset of all patients presenting with an ACS to the ED of 9 participating centers.

Results: Three thousand four hundred sixty four patients of whom 60% were male and 17% were minorities comprised the TRACS registry. Sixty two percent were admitted. The in-hospital mortality rate for admitted patients was 9%. Patients who died in-hospital were older (72 vs 67 y, $p<0.001$), more likely Caucasian (90% vs 82%, $p=.013$), and more likely to have an elevated troponin I (64% vs 46%, $p<0.001$). Conventional risk factors were similar but non-survivors received beta-blockers (36% vs 44%, $p<0.021$), nitrates (27% vs 54%, $p<0.001$), IIb/IIIa platelet blockers (4% vs 13%, $p<0.001$) and IV nitrates in the ED (24% vs 44%, $p<0.001$) less often. Multivariate analysis revealed increased age (odds ratio, 95 CI's: 1.02, 1.01-1.03; $p<0.001$), and an elevated troponin (1.866, 1.32-2.60; $p<0.001$) to be associated with increased mortality while in-hospital IIb/IIIa use (.28, .12-.65; $p=.003$) and IV nitrate use in the ED (.44, .33-.59; $p<0.001$) were associated with reduced mortality.

Conclusion: In this unselected population of admitted acute coronary syndrome patients, mortality was associated with age and elevated troponin levels while in-hospital use of IIb/IIIa platelet blockers and IV nitrate therapy were associated with hospital survivorship. These results reaffirm the prognostic value of age and troponins and the value of more aggressive medical management.

POSTER SESSION

1125 Risk Stratification in Acute Coronary Syndrome

Monday, March 31, 2003, 3:00 p.m.-5:00 p.m.

McCormick Place, Hall A

Presentation Hour: 3:00 p.m.-4:00 p.m.

1125-96

Performance of the Thrombolysis in Myocardial Infarction Risk Index for Early Acute Coronary Syndrome in the National Registry of Myocardial Infarction: A Simple Risk Index Predicts Mortality in Both ST and Non-ST Elevation Myocardial Infarction

Stephen D. Wiviott, David A. Morrow, Robert P. Giugliano, Paul D. Frederick, Carolyn H. McCabe, Christopher P. Cannon, Elliott M. Antman, Eugene Braunwald, Brigham & Women's Hospital, Boston, MA

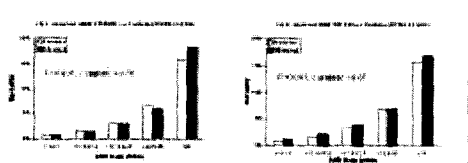
Background: A simple risk index (heart rate \times [Age/10]²/SBP) developed from patients with ST elevation myocardial infarction (STEMI) accurately predicts mortality in clinical trials of fibrinolysis, but has not been evaluated in a general population with STEMI or non-ST elevation MI (NSTEMI).

Methods: To evaluate the TIMI Risk Index (TRI) in such a population in the US, we tested it in the National Registry of Myocardial Infarction (NRFMI) 3 and 4. NRFMI patients were divided into pre-defined risk groups based on the derivation set from patients receiving fibrinolysis in INTIME II.

Results: 117,676 patients with STEMI and 238,815 with NSTEMI were eligible for analysis. NRFMI STEMI patients had a higher risk profile than those in the derivation set (Median TRI: 27 vs. 20). Division of those with STEMI into 5 pre-defined risk groups

revealed a strong graded mortality relationship (Range: 1.0 to 23.1%, $p < .0001$, c-statistic 0.73). The predictive capacity of the TRI was particularly strong in those receiving reperfusion therapy (STEMI-IRS, Fig A). Moreover, in patients with NSTEMI, the risk index also revealed a significant graded relationship with mortality (Fig B).

Conclusions: A simple risk index from baseline clinical variables routinely obtained at the first patient encounter predicted mortality in a heterogeneous group of patients presenting with STEMI or NSTEMI. Despite differences in syndrome pathophysiology, this risk index may prove valuable in the assessment of patients with STEMI or NSTEMI.



1125-97

Thrombolysis in Myocardial Infarction Risk Score and ST Resolution Are Independent Predictors of Mortality

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Background: Previous studies confirmed ST segment resolution (RST) during fibrinolytic therapy (FT) for ST elevation myocardial infarction as a convenient marker of reperfusion correlated to TIMI flow grade and TIMI myocardial perfusion grade. The RST at 60, 90 and 180 min after reperfusion therapy is known to identify low mortality group of patients. The TIMI risk score is a clinical, bedside, risk score developed to predict STEMI 30 days mortality.

Objectives: The aim of this study is to assess the relationship between TIMI risk score and 60 min RST.

Method: A cohort of 728 patients were given pre-hospital FT for STEMI (pain to FT, mean time 120 min). ECG was performed prior starting FT (baseline ECG) and 60 min later. ECG were analyzed to isolate two classes of RST: no or worsening RST (<30%) and partial or complete RST (>=30%). TIMI risk score was calculated at pre-hospital presentation. 30 days mortality was investigated for each class of RST and each level of TIMI risk score.

Results: The results are shown in the table below, and expressed in number of patients. TIMI risk score and 60 min RST are independent 30 days mortality markers ($p > 0.05$).

Conclusion: The absence of relationship between TIMI risk score and 60 min RST for STEMI patients suggests that RST should be taken into account as an independent variable in a new scoring system.

TIMI Risk Score	Death	No RST	RST	Total
0	1	29	71	100
1	4	76	120	196
2	5	41	80	121
3	9	39	79	113
4	12	39	50	89
5	6	22	26	48
6	5	14	14	28
7	4	11	7	18
>=8	5	8	7	15
Total	51	279	449	728

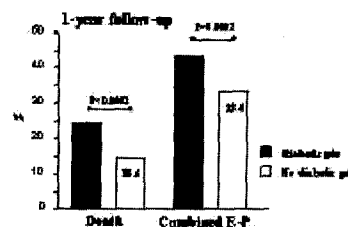
1125-98

One-Year Outcome of High-Risk Patients With Acute Myocardial Infarction With or Without Diabetes: Data From the MISTRAL Study

Samuele Baldasseroni, Giuseppe Steffenino, Francesco Chiarella, Giovanni Maria Santoro, Antonio L. Bartorelli, Maria Luisa Laudisa, Donata Lucci, Aldo P. Maggioni, on behalf of MISTRAL Investigators, ANMCO Research Center, Florence, Italy

Pts with diabetes (D) have more often severe coronary arteriosclerosis with high risk (HR) of AMI and cardiac death. We studied in-hospital and 1-year outcomes of HR pts with AMI with or without D treated with reperfusion therapy (thrombolysis or primary-PCI) or drug therapy. 2227 HR-pts with AMI <12 h were recruited at 17 centres with, and 30 without, feasibility of performing primary PCI (classified at HR having ≥ 1 of the following characteristics: female >70 y, diabetic >70 y, Killip class >1, SBP <100 mmHg and heart rate >100 b/m, >4 leads with ST deviation, previous Q-wave AMI, contraindication to thrombolysis). 1795 pts (80.6%) had not D and 432 pts (19.4%) were diabetic: pts with D were more often females, older, with a history of cardiovascular disease, arrhythmias during hospital stay and heart failure at entry. Pts with D were less treated with reperfusion therapy (74.3% vs 83.0%, $p < 0.0001$) and with betablockers at discharge (41.2% vs 49.5%, $p < 0.005$). One year mortality and combined end-point (death+reAMI+heart failure+angina) are showed in the figure. When we adjusted the 1-year outcomes for all clinical, haemodynamic variables and therapy, D remained an independent prognostic predictor (death OR: 1.54, 95%CI 1.13-2.09; combined end-point OR: 1.13, 95%CI 0.89-

1.43). This study confirms, in a large unselected cohort of HR-pts with AMI, that D is a significant independent predictor of poor prognosis. Nevertheless, pts with D are often undertreated with aggressive mechanical or pharmacological therapy.



1125-99

Unraveling the Spectrum of Left Bundle Branch Block in Acute Myocardial Infarction: Insights From ASSENT 3

Hassam F. Al-Faleh, Yuling Fu, Galen S. Wagner, Shaun G. Goodman, E. Sgarbossa, Christopher B. Granger, Frans J. Van de Werf, Lars Wallentin, Paul W. Armstrong, For the ASSENT 3 Investigators, University of Alberta, Edmonton, AB, Canada

Left bundle branch block (LBBB) complicates AMI diagnosis. Sgarbossa's criteria developed from GUSTO 1 to surmount this diagnostic challenge but have not been previously validated in a clinical trial. We evaluated their utility in the diagnosis and risk stratification of AMI patients (pts) in ASSENT 3. **Methods:** Baseline ECGs of ASSENT 3 pts were reviewed for LBBB by blinded core labs. Sequential ECGs (baseline, 60, 180 min & discharge) of LBBB pts were scored using Sgarbossa's criteria (0-5) for AMI diagnosis. **Results:** 92 (1.5%) pts had LBBB on baseline ECG: their 30-day death vs those without LBBB ($n = 5932$) was 14.1% vs 5.8% respectively ($p = 0.003$). More pts without peak CK ≥ 2 x upper normal limit (UNL) had LBBB than those without LBBB (33.3% vs. 15.7%, $p < 0.001$). Among 75 LBBB pts with peak CK data available, 30 day death tended to be lower among pts without peak CK rise than those with CK rise (4% versus 18%, $p = 0.15$). The table shows Sgarbossa's score of ≥ 3 distribution (highly suggests AMI in the presence of LBBB) and mortality. Sequential ECGs revealed that among 25 LBBB pts without peak CK rise, 15 pts did not have acute MI on admission.

	Sgarbossa score ≥ 3 N=28	Sgarbossa score <3 N=47	P value
Peak CK <2x	2 (7.2%)	23 (48.9%)	<0.001
Peak CK ≥ 2 x and ≤ 3 x		7 (14.9%)	
Peak CK >3x and ≤ 5 x	3 (10.7%)	7 (14.9%)	
Peak CK >5x	23 (82.1%)	10 (21.3%)	
30 day mortality	6/28 (21.4%)	4/47 (8.5%)	0.161

Conclusion: Our findings validate the utility of Sgarbossa's criteria for diagnosing AMI in the setting of LBBB. Sgarbossa's criteria provide a simple and practical diagnostic approach to optimize risk-benefit of acute therapy in this diagnostically challenging group and contribute usefully to risk stratification in this high risk population.

POSTER SESSION

1126 Unstable Angina/Acute Myocardial Infarction: Prognosis

Monday, March 31, 2003, 3:00 p.m.-5:00 p.m.

McCormick Place, Hall A

Presentation Hour: 3:00 p.m.-4:00 p.m.

1126-100

Increase in Mortality of Patients Discharged With the Diagnosis of Acute Myocardial Infarction Between 1986 and 1996

John B. Kostis, Alan C. Wilson, Janet Lawrence-Nelson, Rajiv Ranjan, Nora M. Cosgrove, Clifton R. Lacy, Pearl D'Sa, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, NJ

Background: In-hospital mortality of acute myocardial infarction (MI) has declined in the last 15 years. This study focuses on the outcome of patients after discharge.

Methods: Using a statewide MI database, we examined post-discharge mortality among 30,341 MI patients who were hospitalized in New Jersey from 1986 and 1996.

Results: In 1996 patients were older and more likely to have non-Q MI, revascularization, comorbidity and shorter length of stay. Age adjusted one year mortality after discharge was higher in 1996 compared with 1986 (RR 1.08, 95% CI 1.01-1.16). The increase persisted after adjustment for demographics, comorbidities, complications, procedures and age of infarction (RR 1.54, 95% CI 1.42-1.67). The increased post-discharge mortality diminished the benefit of the marked decline of in-hospital mortality from 3.9% absolute